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IFW/S

PTO/SB/21 (09-04)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

| | |
|------------------------|------------------|
| Application Number | 10/601,242 |
| Filing Date | 06/20/2003 |
| First Named Inventor | Phillip Dan Cook |
| Art Unit | 1635 |
| Examiner Name | Janet Epps Ford |
| Attorney Docket Number | ISIS-5213 |

Total Number of Pages in This Submission

ENCLOSURES (Check all that apply)

| | | |
|--|--|---|
| <input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input checked="" type="checkbox"/> Amendment/Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input checked="" type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Reply to Missing Parts/ Incomplete Application <input type="checkbox"/> Reply to Missing Parts under 37 CFR 1.52 or 1.53 | <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation <input type="checkbox"/> Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____ <input type="checkbox"/> Landscape Table on CD | <input type="checkbox"/> After Allowance Communication to TC <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please Identify below): |
| Remarks | | |

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | | | |
|--------------|----------------------------|----------|--------|
| Firm Name | Isis Pharmaceuticals, Inc. | | |
| Signature | | | |
| Printed name | Jason D. Ferrone, J.D. | | |
| Date | 3/10/2006 | Reg. No. | 52,887 |

CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

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| | | | |
|-----------------------|---------------|------|---------|
| Signature | | | |
| Typed or printed name | Pamela Grooms | Date | 3/10/06 |

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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PTO/SB/17 (12-04)

Approved for use through 07/31/2006. OMB 0651-0032

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Effective on 12/08/2004.

Fees pursuant to the Consolidated Appropriations Act, 2005 (H.R. 4818).

FEE TRANSMITTAL For FY 2005

Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT (\$180.00)

Complete if Known

| | |
|----------------------|------------------|
| Application Number | 10/601,242 |
| Filing Date | 06/20/2003 |
| First Named Inventor | Phillip Dan Cook |
| Examiner Name | Janet Epps Ford |
| Art Unit | 1635 |
| Attorney Docket No. | ISIS-5213 |

METHOD OF PAYMENT (check all that apply)

| | | | | |
|--|--------------------------------------|---|-------------------------------|---|
| <input type="checkbox"/> Check | <input type="checkbox"/> Credit Card | <input type="checkbox"/> Money Order | <input type="checkbox"/> None | <input type="checkbox"/> Other (please identify): _____ |
| <input checked="" type="checkbox"/> Deposit Account | | | Deposit Account Number: | 50-0252 |
| Deposit Account Name: Isis Pharmaceuticals, Inc. | | | | |
| For the above-identified deposit account, the Director is hereby authorized to: (check all that apply) | | | | |
| <input type="checkbox"/> Charge fee(s) indicated below | | <input type="checkbox"/> Charge fee(s) indicated below, except for the filing fee | | |
| <input checked="" type="checkbox"/> Charge any additional fee(s) or underpayments of fee(s) under 37 CFR 1.16 and 1.17 | | <input type="checkbox"/> Credit any overpayments | | |

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

FEE CALCULATION

1. BASIC FILING, SEARCH, AND EXAMINATION FEES

| Application Type | FILING FEES | | SEARCH FEES | | EXAMINATION FEES | | Fees Paid (\$) |
|------------------|-------------|--------------|-------------|--------------|------------------|--------------|----------------|
| | Fee (\$) | Small Entity | Fee (\$) | Small Entity | Fee (\$) | Small Entity | |
| Utility | 300 | 150 | 500 | 250 | 200 | 100 | |
| Design | 200 | 100 | 100 | 50 | 130 | 65 | |
| Plant | 200 | 100 | 300 | 150 | 160 | 80 | |
| Reissue | 300 | 150 | 500 | 250 | 600 | 300 | |
| Provisional | 200 | 100 | 0 | 0 | 0 | 0 | |

2. EXCESS CLAIM FEES

Fee Description

Each claim over 20 or, for Reissues, each claim over 20 and more than in the original patent

Small Entity

Fee (\$)

25

Each independent claim over 3 or, for Reissues, each independent claim more than in the original patent

100

200

180

Multiple dependent claims

| Total Claims | Extra Claims | Fee (\$) | Fee Paid (\$) | Multiple Dependent Claims |
|--------------|--------------|----------|---------------|---------------------------|
| - 20 or HP = | x | = | | Fee (\$) |

HP = highest number of total claims paid for, if greater than 20

| Indep. Claims | Extra Claims | Fee (\$) | Fee Paid (\$) | |
|---------------|--------------|----------|---------------|--|
| - 3 or HP = | x | = | | |

HP = highest number of independent claims paid for, if greater than 3

3. APPLICATION SIZE FEE

If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).

| Total Sheets | Extra Sheets | Number of each additional 50 or fraction thereof | Fee (\$) | Fee Paid (\$) |
|--------------|--------------|--|----------|---------------|
| - 100 = | / 50 = | (round up to a whole number) x | = | |

4. OTHER FEE(S)

Non-English Specification, \$130 fee (no small entity discount)

Other: IDS

Fees Paid (\$)

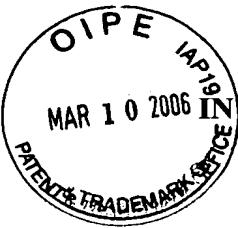
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SUBMITTED BY

| | | | |
|-------------------|------------------------|---|--------------------------|
| Signature | | Registration No. (Attorney/Agent) 52,887 | Telephone (760) 931-9200 |
| Name (Print/Type) | Jason D. Ferrone, J.D. | Date 3/10/2006 | |

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NUMBER: **10/601,242**
FILING DATE: **06/20/2003**
FIRST NAMED INVENTOR: **Phillip Dan Cook**
ART UNIT: **1635**
EXAMINER NAME: **Janet Epps Ford**
ATTORNEY DOCKET NUMBER: **ISIS-5213**

TITLE: GAPPED 2' MODIFIED OLIGONUCLEOTIDES

I certify that this communication is being deposited with the U.S. Postal Service as Express Mail in an envelope addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

Dated: 3/10/06 By: Pamela Grooms
Pamela Grooms

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P.O. BOX 1450
ALEXANDRIA, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT
Under 37 C.F.R. §§ 1.56 and 1.97-98

SIR:

Pursuant to the provisions of 37 C.F.R. §§ 1.56 and 1.97-98, enclosed herewith is PTO Form PTO/SB/08A and PTO/SB/08B listing references for consideration by the Examiner.

The filing of this Information Disclosure Statement shall not be construed as a representation regarding the completeness of the list of references, or that inclusion of a reference in this list is an admission that it is prior art or is pertinent to this application, or that a search has been made, or as an admission that the information listed is, or may be considered to be, material to patentability, or that no other material information exists, and shall not be construed as an admission against interest in any manner.

03/14/2006 WABDELRI 00000080 500252 10601242

01 FC:1806 180.00 DA

This Information Disclosure Statement is being filed:

- within three months of the filing date of the application, or date of entry into the national stage of an international application, or before the mailing date of a first office action on the merits, whichever event last occurred;
- before the mailing of a first official action after filing of a request for continued examination (RCE) under 37 C.F.R. § 1.114;
- after three months of the filing date of this national application or the date of entry of the national stage in an international application, or after the mailing date of the first official action on the merits, whichever event last occurred, but before that mailing date of the first office action to occur of either: (1) a final action under 37 C.F.R. § 1.113; or (2) an action that otherwise closes prosecution in the application, and:
 - attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR
 - Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:
 - each item of the information contained in this Information Disclosure Statement was first cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement; OR
 - no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement.
- on or before the payment of the issue fee but after the mailing date of the first to occur of either: (1) a final action under 37 C.F.R. § 1.113; (2) a notice of allowance under 37 C.F.R. § 1.311; or (3) an action that otherwise closes prosecution in the application, and:
 - Applicant certifies pursuant to 37 C.F.R. § 1.97(e) that:

each item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this statement;
OR
 no item of information contained in this Information Disclosure Statement was cited in a counterpart foreign application and, to the knowledge of the person signing this certification after making reasonable inquiry, no item of information contained in this Statement was known to any individual designated under 37 C.F.R. § 1.56(c) more than three months prior to the filing of this Statement. AND
 attached hereto is the fee set forth under 37 C.F.R. § 1.17(p) for submission of this Information Disclosure Statement under 37 C.F.R. § 1.97(c); OR
 after the payment of the issue fee. Applicant requests that the information contained in this Information Disclosure Statement be placed in the file according to 37 C.F.R. § 1.97(i), although the information may not be considered by the USPTO.

Enclosed is a copy of each listed reference that may be material to the examination of this application, and for which there may be a duty to disclose.

This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior application No. , filed on , and the references cited therein are hereby referenced, but are not required to be provided in this application under 37 C.F.R. § 1.98(d).

This application was filed after June 30, 2003. Therefore, pursuant to the waiver of the requirements under 37 C.F.R. § 1.98(a)(2)(i), copies of each U.S. Patent and each U.S. Patent Application Publication are not required to be submitted. Copies of any foreign patent documents and non-patent literature cited herein are enclosed.

Each item of information contained in this Information Disclosure Statement was cited in the communication from a foreign patent office in a counterpart application, and the communication was not received by any individual designated in 37 C.F.R. §

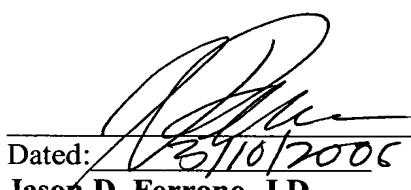
1.56(c) more than thirty days prior to the filing of this Information Disclosure Statement 37 C.F.R. § 1.704(d).

Applicant submits that no fee is required for the consideration of this Information Disclosure Statement. However, if a fee is due, the Commissioner is hereby authorized to charge Deposit Account No 500252 referencing case number

Consideration of the listed references and favorable action are solicited.

Respectively Submitted,

Dated:


3/10/2006
Jason D. Ferrone, J.D.
Registration No.: **52,887**
Isis Pharmaceuticals, Inc.
1896 Rutherford Road
Carlsbad, CA 92008



PTO/SB/08a (08-03)

Approved for use through 07/31/2006. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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~~MARK 5~~ Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 2

| <i>Complete if Known</i> | |
|-------------------------------|-------------------------|
| <i>Application Number</i> | 10/601,242 |
| <i>Filing Date</i> | 06/20/2003 |
| <i>First Named Inventor</i> | Phillip Dan Cook |
| <i>Art Unit</i> | 1635 |
| <i>Examiner Name</i> | Janet Epps Ford |
| <i>Attorney Docket Number</i> | ISIS-5213 |

U.S. PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS

| | | | |
|-----------------------|--|--------------------|--|
| Examiner Signature | | Date Considered | |
|-----------------------|--|--------------------|--|

***EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.¹ Applicant's unique citation designation number (optional).² See *Kinds Codes of USPTO Patent Documents* at www.uspto.gov or MPEP 901.04.³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3).⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document.⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible.⁶ Applicant is to place a check mark here if English language Translation is attached.

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| | | | |
|--|---|-----------------------------|-------------------------|
| Substitute for form 1449B/PTO | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT | | <i>Application Number</i> | 10/601,242 |
| | | <i>Filing Date</i> | 06/20/2003 |
| | | <i>First Named Inventor</i> | Phillip Dan Cook |
| | | <i>Art Unit</i> | 1635 |
| | | <i>Examiner Name</i> | Janet Epps Ford |
| (Use as many sheets as necessary) | | | |
| Sheet | 2 | Of | 2 |
| <i>Attorney Docket Number</i> | | | |
| ISIS-5213 | | | |

NON PATENT LITERATURE DOCUMENTS

| | | | |
|-----------------------|--|--------------------|--|
| Examiner Signature | | Date Considered | |
|-----------------------|--|--------------------|--|

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22213-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22213-1450.